

(FILE 'HOME' ENTERED AT 10:57:56 ON 15 SEP 2006)

FILE 'MEDLINE, CAPLUS, SCISEARCH' ENTERED AT 10:58:10 ON 15 SEP 2006

L1 35 S MANF  
L2 1 S L1 AND PARKINSONS  
L3 0 S MESEMPHALIC (A) ASTROCYTE (2A) NEUROTROPHIC (A) FACTOR  
L4 10 S MESENCEPHALIC (A) ASTROCYTE (2A) NEUROTROPHIC (A) FACTOR  
L5 5 DUP REM L4 (5 DUPLICATES REMOVED)  
L6 0 S L5 AND PY<=2002  
L7 24 S MANF AND PY<=2002  
L8 21 DUP REM L7 (3 DUPLICATES REMOVED)  
L9 1 S L7 AND NEUROTROPHIC  
L10 1 S L7 AND NEURON  
L11 0 S L7 AND MAMMALIAN  
L12 28980 S SAARMA?/AU OR LAUREN?/AU OR LINHOLM?/AU OR TIMMUSK?/AU OR TUO  
L13 0 S L12 AND L7  
L14 0 S L12 AND L1  
L15 1 S L4 AND L12  
L16 37661 S SAARMA?/AU OR LAUREN?/AU OR LINDHOLM?/AU OR TIMMUSK?/AU OR TU  
L17 0 S L16 AND L1  
L18 1 S L16 AND L4  
L19 945 S ARGININE (A) RICH (2A) PROTEIN  
L20 3 S L19 AND MESENCEPHALIC

=> dup rem 120

PROCESSING COMPLETED FOR L20

L21 1 DUP REM L20 (2 DUPLICATES REMOVED)

=> d ibib abs

L21 ANSWER 1 OF 1 MEDLINE on STN DUPLICATE 1  
ACCESSION NUMBER: 2003268334 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 12794311  
TITLE: MANF: a new mesencephalic, astrocyte-derived  
neurotrophic factor with selectivity for dopaminergic  
neurons.  
AUTHOR: Petrova Penka; Raibekas Andrei; Pevsner Jonathan; Vigo  
Noel; Anafi Mordechai; Moore Mary K; Peaire Amy E; Shridhar  
Viji; Smith David I; Kelly John; Durocher Yves; Commissiong  
John W  
CORPORATE SOURCE: Laboratories of Protein Chemistry, Molecular Biology & Cell  
Biology, Prescient NeuroPharma Inc., 96 Skyway Avenue,  
Toronto, Ontario, Canada M9W 4Y9.  
SOURCE: . Journal of molecular neuroscience : MN, (2003 Apr) Vol. 20,  
No. 2, pp. 173-88.  
Journal code: 9002991. ISSN: 0895-8696.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200308  
ENTRY DATE: Entered STN: 10 Jun 2003  
Last Updated on STN: 19 Aug 2003  
Entered Medline: 18 Aug 2003

AB We describe the discovery of a novel, 20 kDa, secreted human protein named  
mesencephalic astrocyte-derived neurotrophic factor, or MANF. The  
homologous, native molecule was initially derived from a rat  
mesencephalic type-1 astrocyte cell line and recombinant MANF  
subcloned from a cDNA encoding human arginine-rich  
protein. MANF selectively protects nigral dopaminergic neurons,  
versus GABAergic or serotonergic neurons. The discovery of MANF marks a  
more systematic approach in the search for astrocyte-derived, secreted  
proteins that selectively protect specific neuronal phenotypes. Compared  
to glial cell line-derived neurotrophic factor (GDNF) and brain-derived

neurotrophic factor (BDNF), MANF was more selective in the protection of dopaminergic neurons at lower (0.05-0.25 ng/mL) and middle (0.5-2.5 ng/mL) concentrations: MANF>GDNF>BDNF. GDNF was more selective at higher concentrations (25-50 ng/ml): GDNF>MANF>BDNF. Two domains in MANF of 39-AA and 109-AA respectively, and eight cysteines are conserved from *C. elegans* to man. MANF is encoded by a 4.3 Kb gene with 4 exons, and is located on the short arm of human chromosome 3. The secondary structure is dominated by alpha-helices (47%) and random coils (37%). Studies to determine the localization of MANF in the brains of rat, monkey, and man, as well as the receptor, signaling pathways, and biologically active peptide mimetics are in progress. The selective, neuroprotective effect of MANF for dopaminergic neurons suggests that it may be indicated for the treatment of Parkinson's disease.

## EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L23	1	"10/302172" and "949"	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2006/09/15 10:45
L22	1	"10/302172"	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2006/09/15 10:45
L21	5	"10302172"	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2006/09/15 10:42
L20	4	mesencephalic adj astrocyte-derived neurotrophic adj (protein or polypeptide) and arginine adj2 rich	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2006/09/15 10:42
S44	211	mesencephalic adj astrocyte-derived neurotrophic adj (protein or polypeptide)	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2006/09/15 10:37
L19	134	mesencephalic adj astrocyte-derived neurotrophic adj (protein or polypeptide) and arginine	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2006/09/15 10:37
L18	0	l17 and l1	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2006/09/15 10:37
L17	136	arginine adj rich adj protein	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2006/09/15 10:37
L16	820	arginine adj rich	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2006/09/15 10:37

## EAST Search History

L15	0	parkisons and arginine adj rich	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2006/09/15 10:37
L14	505	parkisons	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2006/09/15 10:37
L13	505	parkison	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2006/09/15 10:37
L12	0	parkisons and arginine adj rich	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2006/09/15 10:37
L11	0	parkisons same arginine adj rich	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2006/09/15 10:36
L10	12	mesencephalic adj5 neurotrophic adj factor and parkinson	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2006/09/15 10:36
L2	1	manf and arginine adj rich	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2006/09/15 10:36
L1	13	mesencephalic adj5 neurotrophic adj factor	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2006/09/15 10:36
S3	1	WO adj "200268638"	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2006/09/15 10:35
L9	1	WO adj "200268638"	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2006/09/15 10:35

## EAST Search History

L8	3	I3 and I6	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2006/09/15 10:34
L7	0	I2 and I3	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2006/09/15 10:34
L6	3	MANF2	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2006/09/15 10:32
S12	1	manf and arginine adj rich	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2006/09/15 10:31
S9	0	MANF2	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2006/09/15 10:31
S8	0	MANF1	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2006/09/15 10:31
S7	1610	Saarma.in. or Lauren.in. or Linholm.in. or Timmusk.in. or Tuominen.in.	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2006/09/15 10:31
S6	8	Drmanac.in. and arginine adj rich	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2006/09/15 10:31
L5	2	MANF1	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2006/09/15 10:31
L4	8	Drmanac.in. and arginine adj rich	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2006/09/15 10:31

## EAST Search History

L3	2329	Saarma.in. or Lauren.in. or Linholm.in. or Timmusk.in. or Tuominen.in.	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2006/09/15 10:31
S17	9	mesencephalic adj5 neurotrophic adj factor	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2006/09/15 10:30
S46	1	wo adj "200119851"	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2006/09/10 20:32
S1	5	"10302172"	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2006/09/10 20:32